UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,410	04/12/2001	Toyohiro Sawada	019941-000510US	3651

20350 7590 11/19/2010

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
11/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/834,410
Filing Date: April 12, 2001
Appellant(s): SAWADA ET AL.

Joseph Snyder
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 8/31/10 appealing from the Office action mailed 1/4/10.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Notices of Appeal have been filed for application nos. 11/463,570 and 11/841,731. An Appeal brief has been filed in application no. 11/841,731.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1, 3, 5-7, 13-15, 18-21 and 24-36 are pending in the application. Claims 2, 4, 8-12, 16, 17, 22 and 23 have been canceled without prejudice. Claims 1, 3, 5-7, 13-15, 18-21 and 24-36 are rejected and are being appealed.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

4,925,675	GIANNINI et al	05-1990
EP 0661045	SAKO	03-1994
EP 0709386	TANIGUCHI	05-1996

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 5-7, 13-15, 18-21 and 24-36 rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Giannini et al (USPN 4,925,674 hereafter '674) in view of Sako et al (EP 0 661 045 hereafter '045) and Taniguchi et al (EP 0 709 386 hereafter '386).

The '674 patent discloses an amoxicillin containing granule formulation where the core granule comprises sucrose and is coated with amoxicillin (col. 5, lin. 3-15). The coated drug core further comprises a binder such as polyvinyl acetate phthalate, not a hydrogel polymer (col. 5, lin. 16). The coated drug core is further coated with a combination of ethylcellulose and polyethylene glycol (col. 5, lin. 45-col. 6, lin. 24). Ethylcellulose is a hydrogel forming polymer and polyethylene glycol is a hydrophilic polymer. The coated cores are compressed into tablets (col. 8, lin. 29-35).

The reference differs in its disclosure of the specific hydrogel polymer. The reference is however silent to the specific fillers, and active agents of the instant claims. These fillers are well known in the art as shown in the '045 patent. Likewise the active agents are well known as seen in the '386 patent.

The '045 reference teaches a compression molded oral formulation comprising a core comprising a drug (pg. 3, lin. 1-29), along with solubilizers that help improve the solubility of the drug in water such as citric acid, tartaric acid, and polyethylene glycol (pg 3, lin. 30-43). The core is coated with a hydrogel formulation comprising a hydrophilic base such as polyethylene glycols (pg. 3, lin. 49-pg. 4, lin. 7) and hydrogel-forming polymers with viscosities not less than 1000 cps in 1% aqueous solution, and molecular weight above 2,000,000 such as polyethylene oxides (pg. 4, lin. 8-51). The formulation further includes yellow iron sesquioxide (pg. 13, lin. 10-15). The drugs include lidocaine, nicardipine, and quindine, agents that are all metabolized by CYP3A4 (pg. 3, lin. 5-25). Upon administration, water is absorbed into the core of the formulation during its stay in the upper intestine, essentially dissolving the core and releasing the drug slowly as it travels to the colon (pg 2, lin. 35-40). The drug is present in the formulation in concentrations from 80-85%, the hydrophilic base is present in concentration from 5-80%, the hydrogel-forming polymer is present in concentration greater than 16% and solubilizing agent that aids in water absorption into the core is present in concentrations from 15-90% (pg. 3 lin. 25-pg. 5, lin. 13). The formulation remains within the digestive tract for up to 12 hours and within that time the formulation dissolves 70-100% (figures). The reference establishes the level of skill in the art regarding specific fillers and their relation to compression coatings and hydrogel-forming compression tablets. The artisan of ordinary skill would have been able to include the fillers of the '045 reference into the '674 since both formulation disclose similar formulations.

The '386 patent discloses a fused benzazepine derivative, which can be useful as a vasopressin antagonist. The drug can be formulated into tablets using conventional excipients

such as sucrose, gelatin and hydroxypropylcellulose (pg. 27, lin. 23 – 37). The drug of the invention can be used in the treatment of various disorders ranging from cerebrovascular disease to renal disorders (pg. 23, lin. 24 – 44). A skilled artisan would be able to include the compound of '386 into the formulation of '674 since the '674 reference uses similar drugs to treat similar disorders.

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

Regarding the concomitant drug administration, the '674 patent discloses a formulation comprising multiple drug cores, each of which is coated with the same mixture of the hydrophilic and hydrogel forming polymers. These drugs would be separated by the same coating as the instant claims and as such would have the same cocomitant and *in vivo* properties of the instant claims.

Regarding the percentage erosion of the filler, it is the position of the Examiner that this percentage would be inherent to any filler meeting the limitations of the claims. Sucrose and lactose are named in the specification as capable and useful fillers, thus these filler, present in the prior art would act identically and erode to the given percentage. Applicant is invited to provide evidence as to how the sucrose of the instant claims would behave differently than the sucrose of the prior art. Further no temporal data is given regarding when or where the eroding takes place.

Any filler will erode 40-90% given enough time in the digestive tract, regardless of coating and presentation.

Regarding the claim reciting the determination of the eroding percentage, it is the position of the Examiner that the limitations render the claim a product by process claim. The claim is drawn to a tablet, yet recited methods of determination. Also regarding the compression coated limitation, it is the position of the Examiner that such a limitation is merely a product by process limitation, describing the manner in which the tablet is formed. Applicant is reminded that regarding product-by-process claims, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

With these thing in mind it would have been obvious to combine the prior art in order to provide a stable controlled release formulation with improved lower digestive tract release. Following the suggestions of the '674 patent to coat the core tablet with a mixture of polyethylene glycol and oxide, it would have been obvious to use the fillers of the '045 patent in order to provide proper release of the core active agents. It would have been obvious to substitute the active agent of the '386 patent into the combination. One of ordinary skill in the art would have been motivated to combine the suggestions and teachings of the prior art with an expected result of a stable controlled release formulation useful in alleviating undesirable drug interactions.

(10) Response to Argument

Applicant's arguments filed 8/31/10 have been fully considered but they are not persuasive. Applicant argues that the combination of the '674, '045 and '386 patents does not obviate the instant claims because: (A) The '674 patent teaches microgranules and not a tablet as recited in the instant claims; (B) The coatings of the '674 patent are designed for different function than the instant invention; (C) the core of the '674 patent does not contain a drug; (D) the '045 and '386 patent do not meet these deficiencies; and (E) there is no motivation to combine.

Regarding these arguments, it remains the position of the Examiner that the combination of the '674, 045 and '386 patents continues to obviate the instant claims. Regarding the "timed release" limitation in the preamble, applicant argues that this preamble limitation imparts limitations from the specification regarding specific mechanics of the hydrogel swelling and erosion of the coating. Applicant argues that these mechanisms must be taken into consideration with regard to the prior art. In response it remains the position of the Examiner that the combination of cited art in obviating the instant claims also would teach these limitations.

First regarding (A), the '674 patent discloses coated microgranules that are collected and compressed into tablets (col. 8, lin. 28-35). These compression formed tablets would comprise cores and outer coating on said cores. The claims do not specify the size or shape of the "tablet" only that they act as cores that comprise a drug and an erodible filler. This is met by the disclosures of the '674 patent at col. 5, lin. 5-15, where an active agent coating is applied to an inert seed. This would act as the core comprises each element of claim 1(a), specifically core comprising a drug and at least one erodible filler such as sucrose (the seed core) and

polyethylene glycol (binder). These cores further comprises an outer coating that does not comprise a drug and is suggestive of the coating of claim 1(b), specifically the hydrogel forming polymer (ethylcellulose) and the hydrophilic base polyethylene glycol. These coated granules are collected and compressed into a tablet as discussed above. The '674 patent is not meant to be anticipatory and is included in an obviousness rejection because it does not disclose the specific hydrogel forming polymer of the instant claims, nor the specific drug. However the patent establishes the level of skill in the art regarding coating cores comprising a drug and an erodible filler coated with a combination of polymers, specifically a hydrogel former and a hydrophilic base in order to provide precise controlled release of the core drug. The '045 patent provides the specific combination of hydrophilic base polymers and hydrogel-forming polymers suggested in the '674 patent. Both patents provide precise controlled release of active agents, and the coating of the '674 would provide a stable sustained release with specific targeted reels in the GI tract. These coating would have increased to bioavailability of any drug in the formulation and would have been an obvious combination.

Regarding (B), applicant argues that the coating of the '674 patent are designed for a different purpose than that of the instant claims. Again the '674 patent is applied as an obviating reference that discloses the general conditions of a coated drug core, where the core comprises an erodible filler and the coating comprising a hydrogel forming agent and a hydrophilic agent. The specific coating polymers along with their mechanics are taught by the '045 patent. Water permeated the coating gelling the core as it travel along the GI tract [0009-0012]. This property would be inherent to the coating as it comprises the same components, in the same ratio and

applied in the same way as the instant claims. This combination would have the same release mechanics including erosion and gelation due to the identically disposed polymeric components.

Regarding (C) as discussed above the drug/binder layer applied to a sugar (sucrose) seed would constitute the core of claim 1(a). The claim is written with open claim language that the core simply *comprises* a drug and an erodible filler. The claim does not further disclose any specific disposition of the core components other than the components being coated by an outer layer. As such any combination of components including but not limited to a drug and binder coated to a sugar bead, would meet the limitations of the core. The binder can be polyethylene glycol and the bead is sucrose. This would make a core comprising two (2) erodible filler and a drug, meeting the limitations of the instant claim 1(a).

Regarding (D) and (E), as discussed above the ‘674 patent provides the general conditions of the instant claims but is deficient in the specific outer coating hydrogel polymer and the specific drug, though the reference discloses antibiotics, some of which meet the drug limitations of the claims. The ‘045 patent meets the drug and coating deficiencies by disclosing an outer coating that is similar to that of the '674 patent, while disclosing the same polymer combination of the instant claims. Further the drugs recited in the '045 patent, some of which are antibiotics can be metabolized by cytochrome P-450. The ‘386 patent provides the specific fused benzazepine derivative, and discloses that an oral formulation would comprise erodible filler, hydrophilic bases and hydrogel forming polymers. It would have been obvious to combine the specific drug into the combination of the '674 and '045 patent in order to increase its bioavailability. The motivation to makes these combination would come from the fact that the ‘674 and ‘045 patent both operate within the same filed of endeavor and comprises similar

coating and core components. The artisan of ordinary skill would have been motivated to combine the coating of the '045 patent to the similar coating of the '674 patent since the coating would have provide stable, steady and precise sustained release of the drug load along the GI tract. The coating would have provided increase bioavailability and precise control, prompting the artisan of ordinary skill to include the specific fused benzazepine derivative of '386 into the formulation to improve its bioavailability.

For these reasons the claims remain obviated.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/MICAH-PAUL YOUNG/

Examiner, Art Unit 1618

Conferees:

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616